recovering the stem cells from the feeder layer;

said method comprising growing the stem cells under culture conditions that induce somatic differentiation, wherein said conditions do not permit continued stem cell renewal but do not kill stem cells or induce their unidirectional differentiation into extraembryonic lineages.

REMARKS

In the Official Action dated May 22, 2002, claims 19-26 and 37-44 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Thomson et al. (1998) Science 282:1145-1147 (hereinafter "Thomson et al. (Science)"). Claims 19-26 and 37-44 have also been rejected under 35 U.S.C. §102(e) as allegedly anticipated by Thomson, U.S. Patent No. 6,200,806 (hereinafter "Thomson").

This response addresses each of the Examiner's rejections. Accordingly, the pending claims are in condition for allowance. Favorable consideration is respectfully requested.

The Examiner alleges that Thomson et al. (Science) disclose "various culturing methods to differentiate cell lines". Applicants respectfully submit that Thomson et al. (Science) fails to teach or suggest the invention, as claimed. Applicants submit that Thomson et al. (Science) teach spontaneous differentiation of stem cells and not directed differentiation, as claimed. The Examiner's attention is respectfully directed to Thomson et al., (Science) page 1146, second full paragraph wherein Thomson notes that "when [ES cells are] grown to confluence and allowed to pile up in the culture dish, the ES cell lines differentiated spontaneously even in the presence of fibroblasts". In contrast, the present invention, as claimed, is drawn to a method of directing somatic differentiation by culturing cells under

conditions which, inter alia, do not induce extraembryonic differentiation. Moreover, Thomson et al. (Science) do not disclose the generation of differentiated somatic lineages of a non-extraembryonic type *in vitro*. Accordingly, Applicants respectfully submit that Thomson et al. (Science) do not teach each and every element of the claimed invention and withdrawal of the rejection of claims 19-26 and 37-44 under 35 U.S.C. §102(b) is therefore respectfully requested.

Claims 19-26 and 37-44 have also been rejected under 35 U.S.C. §102(e) as allegedly anticipated by Thomson. Applicants respectfully submit that Thomson fails to teach or suggest the claimed invention. Applicants submit that it is well established that for reference to be cited against a claimed invention, the reference itself must be enabling. *Akzo, N.V.U. USITC*, 808 F.2d 1471, 1479 (Fed. Cir. 1986) cert. denied 482 US 909 (1987). Applicants respectfully submit that Thomson is not enabled for directing somatic differentiation of human ES cells per se. Notably, Thomson merely discloses that when cultured in high density, ES cells are capable of differentiating into multiple lineages. However, Thomson fails to enable, no less disclose culture conditions which facilitate differentiation of ES cells into a particular lineage.

Furthermore, the Examiner's attention is directed to column 12, line 50 wherein Thomson discloses extraembryonic differentiation, a condition not permitted by the claimed invention. The Examiner's attention is further directed to, column 12, line 54 which underscores the failure of Thomson to achieve the present invention. Specifically primate ES cells spontaneously differentiate in the culture conditions provided. In stark contrast, the present invention provides directed somatic differentiation into a particular lineage.

Accordingly, the rejection of claims 19-26 and 37-44 under 35 U.S.C. §102(e) is overcome and withdrawal thereof is respectfully requested.

Attached hereto is a marked-up version of the changes made to the claims by the instant amendment. The attached page is captioned "**Version with Markings to Show Changes Made.**"

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 19 has been amended as follows:

19.(Twice Amended) An *in vitro* method of directing [inducing] somatic differentiation of undifferentiated, pluripotent human embryonic stem cells, wherein said undifferentiated, pluripotent human embryonic stem cells are prepared by a process comprising:

obtaining an *in vitro* fertilized human embryo and growing said embryo to a blastocyst stage of development;

removing inner cells mass (ICM) cells from said embryo;

culturing said ICM cells under conditions which do not induce extraembryonic differentiation and cell death and promote proliferation of undifferentiated stem cells; and

recovering stem cells;

said method comprising growing said stem cells under culture conditions that induce somatic differentiation, wherein said conditions do not permit continued stem cell renewal but do not kill stem cells or induce their unidirectional differentiation into extraembryonic lineages.

Claim 37 has been amended as follows:

37.(Amended) An *in vitro* method of directing [inducing] somatic differentiation of undifferentiated, pluripotent human embryonic stem cells, wherein said undifferentiated, pluripotent human embryonic stem cells are prepared by a process comprising:

obtaining an *in vitro* fertilized human embryo and growing the embryo to a blastocyst stage of development;

removing inner cell mass (ICM) cells from the embryo;

culturing ICM cells on a fibroblast feeder layer to obtain proliferation of undifferentiated stem cells; and

recovering the stem cells from the feeder layer;

said method comprising growing the stem cells under culture conditions that induce somatic differentiation, wherein said conditions do not permit continued stem cell renewal but do not kill stem cells or induce their unidirectional differentiation into extraembryonic lineages.